

In the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims

1. (currently amended) An *in vitro* method for screening compounds that modulate the CD40L/CD40R signaling pathway, said method comprising the following steps:

(i) contacting a first sample of cells that express CD40R and β -amyloid precursor protein (β -APP) with CD40 ligand and measuring the level or amount of one or more markers, wherein said one or more markers is the level or amount of one or more of β -amyloid precursor protein (β -APP) or a fragment thereof, which fragment is generated by the proteolytic processing of β -APP by one or more of α -, β - or γ -secretase;

(ii) contacting a second sample of said cells that express CD40R and β -APP ~~neuronal cells~~ with a compound and CD40 ligand and measuring the level or amount of said one or more markers; and

(iii) comparing the level or amount of said one or more markers determined in step (i) with the level or amount of said one or more markers determined in step (ii), wherein a difference in the levels or amounts of the said one or more markers measured in steps (i) and (ii) indicates a compound that modulates the CD40L/CD40R signaling pathway.

2-92. (canceled)

93. (previously presented) The method of claim 1, wherein said compound is a compound that modulates the CD40L/CD40R signaling pathway upstream or downstream of CD40L/CD40R interaction.

94. (previously presented) The method of claim 93, wherein said compound binds to CD40R, binds to CD40L, or interferes with TNF receptor-associated factors.
95. (previously presented) The method of claim 94, wherein said compound binds to CD40R and decreases trimerization of CD40R.
96. (previously presented) The method of claim 94, wherein said compound binds to CD40L and decreases trimerization of CD40L.
97. (currently amended) The method of claim 1, wherein said compound alters β -APP processing.
98. (previously presented) The method of claim 97, wherein said compound modulates presenilin-1 activity, modulates presenilin-2 activity, inhibits β -secretase activity, inhibits γ -secretase activity, or enhances α -secretase activity.
99. (currently amended) The method of claim 93 or 97, wherein said compound reduces the ratio of β -APP β -CTF to β -APP α -CTF, reduces the amount or level of β -CTF, reduces soluble β -amyloid levels, or reduces total β -amyloid levels relative to a control culture.
100. (previously presented) The method of claim 1, 93 or 97, wherein said compound is a soluble CD40R compound or variant thereof, or a soluble CD40L compound or variant thereof.
101. (previously presented) The method of claim 100 wherein said compound is a soluble CD40L compound or variant thereof, which compound is immunogenic.
102. (previously presented) The method of claim 1, 93 or 97, wherein said compound is an interfering or antisense RNA compound to CD40R or CD40L.

103. (previously presented) The method of claim 102 wherein said compound is an interfering RNA compound, which compound is dsRNA, RNAi or siRNA.
104. (previously presented) The method of claim 1, 93, or 97, wherein said compound is an antibody to CD40R.
105. (canceled)
106. (canceled)
107. (previously presented) The method of claim 1, 93, or 97, wherein said compound is an antibody to CD40L.
108. (canceled)
109. (canceled)
110. (currently amended) The method of claim 1, wherein said cells expressing CD40R and β -APP neuronal cells are neurons or neuroblastoma cells.
111. (previously presented) The method of claim 110, wherein said cells are neuroblastoma cells, which cells are N2a cells.
112. (currently amended) The method of claim 1, wherein said cells expressing CD40R and β -APP neuronal cells are derived from a transgenic animal.
113. (currently amended) The method of claim 112, wherein the transgenic animal expresses transgenic β -APP or expresses transgenic tau protein.
114. (previously presented) The method of claim 112, wherein the transgenic animal overexpresses presenilin protein, overexpresses CD40R, or overexpresses CD40L.

115. (currently amended) The method of claim 1, wherein said cells expressing CD40R and β -APP neuronal cells are derived from an animal afflicted with a disease or disorder associated with neuronal inflammation.
116. (previously presented) The method of claim 115, wherein said disease or disorder is an amyloidogenic disease.
117. (previously presented) The method of claim 1, wherein said neuronal cells are derived from an animal afflicted with an amyloidogenic disease.
118. (previously presented) The method of claim 116 or 117, wherein said amyloidogenic disease is Alzheimer's disease, scrapie, transmissible spongiform encephalopathy, hereditary cerebral hemorrhage with amyloidosis Icelandic-type, hereditary cerebral hemorrhage with amyloidosis Dutch-type, familial Mediterranean fever, familial amyloid nephropathy with urticaria and deafness (Muckle-Wells syndrome), myeloma or macroglobulinemia-associated idiopathy associated with amyloid, familial amyloid polyneuropathy (Portuguese), familial amyloid cardiomyopathy (Danish), systemic senile amyloidosis, familial amyloid polyneuropathy (Iowa), familial amyloidosis (Finnish), Gerstmann-Strausler-Scheinker syndrome, medullary carcinoma of thyroid, isolated atrial amyloid, diabetes Type II, or insulinoma.
119. (previously presented) The method of claim 116 or 117, wherein the amyloidogenic disease is a tauopathy.
120. (previously presented) The method of claim 116, wherein said tauopathy is Alzheimer's disease, frontotemporal dementia, frontotemporal dementia with Parkinsonism, frontotemporal lobe dementia, pallidopontonigral degeneration, progressive supranuclear palsy, multiple system tauopathy, multiple system tauopathy with presenile dementia, Wilhelmsen-Lynch disease, disinhibition-dementia-parkinsonism-amyotrophy complex, Pick's disease, or Pick's disease-like dementia.

121. (currently amended) The method of claim 1, wherein said fragment is β -amyloid protein ($A\beta$) ~~or a fragment thereof~~.